510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k061193

B. Purpose for Submission:

New device

C. Measurand:

Creatinine

D. Type of Test:

Quantitative, Colorimetric (absorbance change at 500 nm)

E. Applicant:

Abbott Laboratories

F. Proprietary and Established Names:

Abbott Laboratories Clinical Chemistry Creatinine

G. Regulatory Information:

1. Regulation section:

   21 CFR § 862.1225

2. Classification:

   Class II

3. Product code:

   CGX

4. Panel:

   75 (Clinical Chemistry)

H. Intended Use:

1. Intended use(s):

   A creatinine test system is a device intended to measure creatinine levels in serum, plasma and urine.

2. Indication(s) for use:

   A creatinine test system is a device intended to measure creatinine levels in serum, plasma and urine. Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.

3. Special conditions for use statement(s):

   For professional use.

4. Special instrument requirements:

   Abbott Laboratories Aeroset and Architect *c8000* Systems

I. Device Description:

The Aeroset and Architect *c8000* creatinine assay is a liquid, ready-to-use, two-reagent kit. R1 contains Sodium Hydroxide at a concentration of 0.8 mol/L and R2 contains Picric Acid at a concentration of 25.0 mmol/L. The same reagent kit may be used on either the Aeroset or Architect *c8000* Systems.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Roche creatinine assay

2. Predicate 510(k) number(s):

   k941837

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Assay	Same	Automated Quantitative Measurement of Creatinine
Methodology	Same	Modified Jaffe
Matrices	Same	Serum, Urine, Plasma

Differences		
Item	Device	Predicate
Reportable Range	Serum: 0.20 – 37.00 mg/dL Plasma: 0.20 – 37.00 mg/dL Urine: 5.0 – 740.0 mg/dL	Serum: 0.20 – 25.00 mg/dL Plasma: 0.20 – 25.00 mg/dL Urine: 0.2 – 650 mg/dL

K. Standard/Guidance Document Referenced (if applicable):

CLSI (formerly NCCLS) Document EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition

CLSI (formerly NCCLS) Document EP5-A: Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline

CLSI (formerly NCCLS) Document EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline

CLSI (formerly NCCLS) Document EP10-A: Preliminary Evaluation of Quantitative Clinical Laboratory Methods; Approved Guideline

L. Test Principle:

Abbott Clinical Chemistry Creatinine is an in vitro diagnostic assay for the quantitation of creatinine in human serum, plasma, or urine. At an alkaline pH, creatinine in the sample reacts with picrate to form a creatinine-picrate complex. The rate of increase in absorbance at 500 nm due to the formation of this complex is directly proportional to the concentration of creatinine in the sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*
   Serum Application: The total precision as well as the precision for each component of variation (between-day, between-run, and within-run) was estimated for creatinine. Two control levels (Level 1 and Level 2) at normal and abnormal analyte concentrations were tested. These controls were evaluated over 20 days, two runs per day, and two replicates per run. Precision

was reported as the total percent CV. This study was conducted in accordance with CLSI Document EP5-A. Summary results were as follows:

AEROSET Serum Precision

Control		Level 1	Level 2
N		80	80
Mean (mg/dL)		1.20	4.66
Within Run	SD	0.01	0.03
	%CV	0.76	0.57
Between Run	SD	0.01	0.04
	%CV	0.81	0.80
Between Day	SD	0.06	0.14
	%CV	4.83	3.02
Total	SD	0.06	0.15
	%CV	4.95	3.18

ARCHITECT Serum Precision

Control		Level 1	Level 2
N		80	80
Mean (mg/dL)		1.27	4.81
Within Run	SD	0.02	0.02
	%CV	1.74	0.44
Between Run	SD	0.01	0.04
	%CV	1.01	0.92
Between Day	SD	0.03	0.06
	%CV	2.36	1.15
Total	SD	0.04	0.07
	%CV	3.10	1.54

Urine Application: Five day precision studies were conducted on the AEROSET and ARCHITECT *c8000* Systems in accordance with CLSI Document EP10-A. This study was intended to supplement data obtained from the twenty-day serum precision study and provides a limited assessment of the performance of the assay with the urine matrix. Two control levels (Level 1 and Level 2) at normal and abnormal analyte concentrations were tested for the urine application. These controls were evaluated over five days, two runs per day, and five replicates per run. Precision was reported as the total percent CV.

AEROSET Urine Precision

Control		Level 1	Level 2
N		50	50
Mean (mg/dL)		42.28	92.75
Within Run	SD	0.96	1.80
	%CV	2.26	1.94
Between Run	SD	0.14	1.01
	%CV	0.32	1.09
Between Day	SD	0.32	0.85
	%CV	0.77	0.92
Total	SD	1.02	2.23
	%CV	2.41	2.41

ARCHITECT Urine Precision

Control		Level 1	Level 2
N		50	50
Mean (mg/dL)		42.59	93.91
Within Run	SD	0.37	0.73
	%CV	0.87	0.78
Between Run	SD	0.11	0.56
	%CV	0.25	0.60
Between Day	SD	0.12	0.14
	%CV	0.28	0.15
Total	SD	0.40	0.93
	%CV	0.94	0.99

b. Linearity/assay reportable range:

The sponsor's reportable range for serum and plasma is 0.20 – 37.00 mg/dL and 5.0 – 740.0 mg/dL for urine.

Linearity of the assay across the measuring range was established by measuring serum and urine samples at concentrations spanning the measuring range of the assay in four replicates. At least one level was included which exceeded the desired linear range. To measure the highest concentration sample, the analyzer's "linear high" and ">" error codes were suppressed. The

percent recovery for each sample was determined by dividing the mean observed result by the expected value.

The sponsor also provided data demonstrating equivalence between the analyzer's auto-dilution feature and manual dilutions.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

This assay utilizes the Abbott Multiconstituent Calibrator which was cleared under k981706.

Shelf life, calibration, and on-board stability study protocols and acceptance criteria were described and found to be acceptable.

d. *Detection limit:*

The functional sensitivity of the Creatinine assay was determined based on the Limit of Quantitation (LOQ). To determine the LOQ, test levels near the linear low for the Creatinine assay were run in replicates of 10, on three instruments, two runs per instrument. The limit of quantitation was defined as the lowest concentration of analyte which has imprecision less than or equal to 20% CV. An internal verification study supported an LOQ of 0.10 mg/dL for the serum application and 2.0 mg/dL for the urine application. The (Limit of Detection (LOD) testing for Creatinine was performed using a study design based on CLSI EP17-A. An internal verification study supported an LOD of 0.05 mg/dL for the serum application, and 1.0 mg/dL for the urine application. The proportions of false positives (α) and false negatives (β) were less than 5% and the limit of blank (LOB) was 0.0224 mg/dL for serum and 0.3732 mg/dL for urine.

Conclusions: The LOQ for Creatinine serum is 0.10 mg/dL and the LOD is 0.05 mg/dL. The LOQ for Creatinine urine is 2.0 mg/dL and the LOD is 1.0 mg/dL.

Limit of Detection (Serum)

	Instrument	N	Limit of Blank (mg/dL)	SD	Limit of Detection (mg/dL)
AEROSET	1	20	0.0153	0.0064	0.0258
	2	20	0.0197	0.0100	0.0362
	3	20	0.0081	0.0067	0.0191
ARCHITECT	1	20	0.0108	0.0071	0.0224
	2	20	0.0224	0.0046	0.0300
	3	20	0.0224	0.0051	0.0307

Limit of Quantitation (Serum)

	Instrument	N	Mean (mg/dL)	SD	% CV
AEROSET	1	20	0.0721	0.0093	12.8771
	2	20	0.0713	0.0127	17.8165
	3	20	0.0684	0.0073	10.6171
ARCHITECT	1	20	0.0368	0.0072	19.6566
	2	20	0.0457	0.0058	12.7092
	3	20	0.0506	0.0057	11.2252

Limit of Detection (Urine)

	Instrument	N	Limit of Blank (mg/dL)	SD	Limit of Detection
AEROSET	1	20	0.2557	0.1770	0.5508
	2	20	0.3732	0.1673	0.6484
	3	20	0.2833	0.1301	0.4973
ARCHITECT	1	20	0.3024	0.2009	0.6329
	2	20	0.2856	0.2204	0.6482
	3	20	0.2509	0.2466	0.6565

Limit of Quantitation (Urine)

	Instrument	N	Mean (mg/dL)	SD	% CV
AEROSET	1	20	1.8140	0.1262	6.9579
	2	20	1.7137	0.1741	10.1572
	3	20	0.7340	0.1413	19.2540
ARCHITECT	1	20	1.8112	0.1465	8.0874
	2	20	2.0207	0.2300	11.3821
	3	20	1.8596	0.2018	10.8516

e. Analytical specificity:

Interferents, which may falsely elevate or reduce the concentration of an analyte, were tested. Human serum samples at the medical decision level of the analyte and urine samples were spiked with various levels of interferents. Four replicates of each interferent level and four replicates of an unspiked reference sample were run. The percent recovery was determined by dividing the mean result of each interferent sample by the mean result of the reference sample. Testing was performed using the AEROSET System only.

The percent interference was within ± 10% difference for serum samples containing 30 mg/dL bilirubin; 2,000 mg/dL hemoglobin; 1,000 mg/dL Intralipid; 3.0 mg/dL ascorbate; 300 mg/dL glucose; and 10.6 g/dL protein at Medical Decision Level 1.

The percent interference was within ± 10% difference for serum samples containing 30 mg/dL bilirubin; 2,000 mg/dL hemoglobin; 1,000 mg/dL Intralipid; 3.0 mg/dL ascorbate; 600 mg/dL glucose; and 14.7 g/dL protein at Medical Decision Level 2.

Interfering Substances for Serum - Level 1

Interfering Substance	Interfering Substance Concentration	Target (mg/dL)	Observed (% of Target)
Bilirubin	30 mg/dL	1.549	98.11
	60 mg/dL	1.549	71.87
Hemoglobin	1,000 mg/dL	1.403	104.79
	2,000 mg/dL	1.403	108.86
Intralipid	750 mg/dL	1.425	99.44
	1,000 mg/dL	1.425	98.39
Ascorbate	1.5 mg/dL	1.522	99.49
	3.0 mg/dL	1.522	98.83
Glucose	300 mg/dL	1.522	107.08
	600 mg/dL	1.522	115.92
Protein	10.6 g/dL	1.537	107.97
	14.3 g/dL	1.537	115.37

Interfering Substances for Serum - Level 2

Interfering Substance	Interfering Substance Concentration	Target (mg/dL)	Observed (% of Target)
Bilirubin	30 mg/dL	5.334	94.91
	60 mg/dL	5.334	74.71
Hemoglobin	1,000 mg/dL	4.701	102.07
	2,000 mg/dL	4.701	103.29
Intralipid	750 mg/dL	4.619	98.99
	1,000 mg/dL	4.619	99.10
Ascorbate	1.5 mg/dL	5.230	99.61
	3.0 mg/dL	5.230	99.71
Glucose	300 mg/dL	4.999	101.46
	600 mg/dL	4.999	103.16
Protein	10.8 g/dL	5.571	99.13
	14.7 g/dL	5.571	99.08

The percent difference was within ± 10% for urine samples containing 6.25 mL/dL acetic acid (8.5 N), 200 mg/dL ascorbate, 250 mg/dL boric acid, 1,000 mg/dL glucose, 2.5 mL/dL hydrochloric acid (6 N), 5.0 mL/dL nitric acid (6 N), 50 mg/dL protein, 1.25 g/dL sodium carbonate, 400 mg/dL sodium fluoride, and 60 mg/dL sodium oxalate.

Interfering Substances for Urine

Interfering Substance	Interfering Substance Concentration	Target (mg/dL)	Observed (% of Target)
Acetic Acid (8.5 N)	6.25 ml/dL	95.543	100.10
Ascorbate	200 mg/dL	90.533	99.75
Boric Acid	250 ml/dL	95.035	100.14
Glucose	1,000 mg/dL	94.128	100.39
Hydrochloric Acid (6 N)	2.5 ml/dL	95.043	100.75
Nitric Acid (6 N)	5.0 ml/dL	95.338	99.82
Protein	50 mg/dL	95.470	101.93
Sodium Carbonate	1.25 g/dL	95.805	99.96
Sodium Fluoride	400 mg/dL	96.150	99.78
Sodium Oxalate	60 mg/dL	95.678	100.50

f. Assay cut-off:

Not Applicable.

2. Comparison studies:

a. Method comparison with predicate device:

AEROSET:

The sponsor compared 117 serum samples ranging from 0.69 to 38.36 mg/dL (as measured by the predicate method). Samples with concentrations greater than 25 mg/dL were diluted X2 on the predicate method but run undiluted on the Aeroset. Linear regression produced a slope of 0.98, a y-intercept of -0.18, and a correlation coefficient of 0.995.

The sponsor also compared 50 urine samples ranging from 7.14 to 401.72 mg/dL (as measured by the predicate method). Linear regression produced a slope of 0.94, a y-intercept of -3.66, and a correlation coefficient of 0.999.

ARCHITECT:

The sponsor compared 117 serum samples ranging from 0.69 to 38.36 mg/dL (as measured by the predicate method). Samples with concentrations greater than 25 mg/dL were diluted X2 on the predicate method but run undiluted on the Architect. Linear regression produced a slope of 0.96, a y-intercept of -0.24, and a correlation coefficient of 0.999

The sponsor also compared 50 urine samples ranging from 7.14 to 401.72 mg/dL (as measured by the predicate method). Linear regression produced a slope of 0.93, a y-intercept of -4.16, and a correlation coefficient of 0.999.

b. Matrix comparison:

Serum, lithium heparin plasma, and sodium heparin plasma are recommended as acceptable matrices in the sponsor's labeling. To demonstrate comparable performance, the sponsor compared serum from a plain glass tube (baseline) with serum from a gel tube, lithium heparin plasma, lithium heparin plasma from a gel tube, and sodium heparin plasma. All of the recommended matrices showed acceptable performance.

3. Clinical studies:

a. Clinical Sensitivity:

Not Applicable.

b. Clinical specificity:

Not Applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off**:**

   Not Applicable.

5. Expected values/Reference range:

   The sponsor cites reference ranges from Tietz Fundamentals of Clinical Chemistry, 5th ed, 2001:975.

SERUM/PLASMA	Range (mg/dL)	Range (µmol/L)
Cord	0.6 to 1.2	53 to 106
Newborn, 1 to 4 days	0.3 to 1.0	27 to 88
Infant	0.2 to 0.4	18 to 35
Child	0.3 to 0.7	27 to 62
Adolescent	0.5 to 1.0	44 to 88
Adult, Male	0.7 to 1.3	62 to 115
Adult, Female	0.6 to 1.1	53 to 97

URINE	Range (mg/kg/day)	Range (µmol/kg/day)
Infant	8 to 20	71 to 177
Child	8 to 22	71 to 194
Adolescent	8 to 30	71 to 265
Adult, Male	14 to 26	124 to 230
Adult, Female	11 to 20	97 to 177

(Declines with age to 10 mg/kg/day at age 90)

The sponsor recommends that each laboratory determine its own reference ranges based upon its particular locale and patient characteristics.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.